Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/clinicians-roundtable/opioids-fish-oils-and-hibernating-bears/2953/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Opioids, Fish Oils and Hibernating Bears

Opioids, fish oils, and hibernating beers, how do these relate to the study of heart disease? You are listening to ReachMD XM 157, the channel for medical professionals. Welcome to a special segment on medical education on the clinician's roundtable. I am your host, Dr. Matthew Sorrentino from University of Chicago and joining me today is Dr. Paul Iaizzo. He is the professor in the departments of anesthesia and physiology and the department of surgery, and the Medtronic professor in the Visible Heart Laboratory at the University of Minnesota, Minneapolis, Minnesota.

DR. MATTHEW SORRENTINO:

Dr. Iaizzo, welcome to the show.

DR. IAIZZO:

Thanks for the invite.

DR. MATTHEW SORRENTINO:

The Visible Heart Laboratory at the University of Minnesota is a laboratory where a lot of research is being done on studying heart anatomy and physiology. Can you describe a little bit about how this laboratory is set up and what type of work you are doing?

DR. IAIZZO:

Well! it's a broad ranging lab and we like to think of our lab of doing basically translational systems physiology and the primary focus is on muscle, but that muscle can be skeletal muscle or cardiac muscle, and we work at every level on the lab which is fairly unique. In that, we will do everything from human performance work looking at muscle force, assessment in patients with neuromuscular disorders or normal subjects all the way down to a fresh cadaver work in humans to large animal models for 01:30) various disease states or cardiovascular dysfunctions and also looking at skeletal muscle function to organ work where we do isolated cardiac work down to tissue level work where we will actually get biopsies from patients from the OR, that's skeletal muscle or when they will do a transplant at the U, we will get a portion of the recipient's diseased heart and then all the way down to cellular stuff where we are doing isolated myositis and <_____>.

© 2023 ReachMD

DR. MATTHEW SORRENTINO:

Tell me a little bit about the isolated heart model, how is that type of model set up?

DR. IAIZZO:

Basically, what we are doing in this set up is that we are isolating large <_____> hearts and then reanimating them outside the body and we are doing a lot of methodologies that have been well described in literature. So back in the 1890s, Oscar Langendorff first described basically reanimating hearts and he did so with a blood perfuse aid and uniquely what we are doing in our lab is we are doing a clear perfuse aid which is a <_____> buffer with various additives, but basically meaning there is glucose and insulin and we can also add omega-3 fatty acids, and we can get these hearts to work outside the body in a Langendorff mode, but we can also switch it so that it's fully functional, so it's basically self perfusing itself and therefore feeding its own coronaries and then basically we can do this. It will stay viable for 5-7 hours (03:00) and then we can put high-resolution endoscopes inside these hearts and visualize all the functional anatomy.

DR. MATTHEW SORRENTINO:

So, these are beating hearts. Are they beating at the same speed, the same contractility as you would in vivo?

DR. IAIZZO:

Good question. What's really surprising is that these hearts will all go into a native sinus rhythm and basically though elicited heart rates of 80-90 beats per minute on their own will still respond to catecholamines so you can increase contractility and we can get a cardiac outputs in these hearts from 5-7 liters if we are giving the catecholamines and calcium additives so you can get some really nice functional images from these hearts.

DR. MATTHEW SORRENTINO:

Now, some of the research I know that's being done is seeing how devices interact with tissues and I understand you have got this clear perfuse aid so you can actually take videos of how these devices interact inside the beating heart?

DR. IAIZZO:

Correct. Most interesting aspect of this is now you can actually visualize the device tissue interface and you can see how, for example, a catheter or lead placed through a valve will modify the function of that valve or we can actually implant valves into the heart and these could be mechanical valves or tissue valves, or recently we have been doing deployment of transcatheter delivered valves into (04:30) the heart and then we can see how all those seat within the heart and then although interact with the surrounding tissues during function during the whole complete cardiac cycle and again we can try to up-regulate the heart as best we can to really enhance performance.

DR. MATTHEW SORRENTINO:

© 2023 ReachMD

Have you learned anything about some of device studies that have helped design better devices, better leads, better catheters?

DR. IAIZZO:

Yeah. That's been the collaboration with Medtronic and for years they have brought in a lot other prototype devices and we have seen these devices early on and one of these are in market now. We have also utilized this approach for a training tool so we have had key opinion leaders from all over the world that a lot of these individuals doing the first clinical trials were coming to the lab and perform the procedures in the visible heart and be able to visualize this and we can actually complement the whole study by simultaneously doing standardized imaging with fluoroscopy or echocardiography and so it's a really unique set up. We have also then used this to create educational pieces for physician and resident training on the procedural approaches to putting in new devices.

DR. MATTHEW SORRENTINO:

So you can have simultaneous invasive type hemodynamic parameters as well as noninvasive imaging like echo all in the same setup.

DR. IAIZZO:

Correct. We have gotten to the point where we will have a lot of pressure catheters, sonomicrometry, flow probes (06:00) all within these beating hearts. We have had mapping catheters in there, we have done ablation procedures in these hearts, and all of which you can do multiple imaging simultaneously.

DR. MATTHEW SORRENTINO:

If you are just joining us, you are listening to a special segment on medical education on ReachMD XM 157, the channel for medical professionals. I am your host, Dr. Matthew Sorrentino and I am talking to Dr. Paul Iaizzo and we are discussing the Visible Heart Laboratory at The University of Minnesota.

Some of the work you are doing is on cardiac protection, cardiac preconditioning. Can you describe some of that research for us?

DR. IAIZZO:

Oh sure, I can, but I kind have to set it up how I got into this and it's kind of a round about way in that been doing force studies on patients with neuromuscular disorders for many years and we actually are able to use devices that will measure torque which will stimulate the nerves, which makes the muscles contract, and then we can record the forces, so it's a noninvasive quantitative approach to look at the forces. It was about 10 years ago I was sitting in my office, I got a phone call from Prof. Hank Harlow at the University of Wyoming and Hank said that Hey Paul, this is Hank Harlow, I have read your research on force assessment, which is always a surprise that someone will read all your papers, but then he said very intrigued by it, "would you be interested in collaborating with us, we are looking at a (07:30) population of individuals that do not get weak or elicit weakness even though they are immobilized for 4-6 months." I said "sure, it sounds wonderful" and he says, "well, we are studying hibernating black bears" and I said "fantastic" and I kind of surprised him. Being a Minnesotan and loving the outdoors, I jumped at the opportunity for this. So we actually started doing this work and it turns out that these bears do indeed do not have any muscle loss and it turns out they have a whole cascade of hormones called hibernation induction triggers that will circulate during the winter presumably and induce this hibernation state to actually provide ischemic protection to the vital organs and minimize muscle protein loss and therefore strength, and then we started looking into this, and it turns out that

© 2023 ReachMD

one of the properties of these circulating hormones is their delta opioid agonist. These delta opioid agonists are thought to be agents that will confer protection against the ischemic damage not only of the brain and skeletal muscles, but the heart as well. So, then we began looking at this within various animal models in our lab and one of the things that we did is we applied these delta opioids to an ischemic model where we will do an occlusion of the LAD and then we will look at (09:00) ischemia reperfusion injury and one of the things that we did see with applying this was that the delta opioids reduced the infarct size by 50% in this model and so then we expanded this work to look at delta opioids and their potential for allowing for prolonged preservation of the heart and the ischemic period. We have also done some tissue bath work in our lab with isolated trabeculated from human hearts as well trying to make this all translational.

DR. MATTHEW SORRENTINO:

So it sounds like there is a protective mechanism if you will through the opioid system that can protect the heart when it becomes ischemic. Would this be true using opioids like morphine, for example, would that help with some of these ischemic times in the heart?

DR. IAIZZO:

That's a good question and one that we actually investigated. It turns out that morphine is what we kind of consider a dirty agent to map. It actually lacked of mu, kappa, and delta opioid receptors, and it masked the positive benefits of activity in the delta receptors by activating kappa receptors and so we actually did a study that if you just gave morphine alone, there were no protective benefits, but if you were able to give morphine and a kappa blocker or kappa antagonist, then basically you conferred protection.

DR. MATTHEW SORRENTINO:

So, we are giving the wrong opioid to our patients who come into the ER (10:30) having severe chest pain and having a myocardial infarction.

DR. IAIZZO:

Well, you are giving a neutral agent. You are not benefiting, but you are not hurting them either. If you were just to give a kappa, you may actually worsening the situation, but the goal is to try to make this translation in the future and figure out if we can look at this pharmacology and then really provide the right opioids at the right time.

DR. MATTHEW SORRENTINO:

Now I understand you are doing some work with lipids as well in preconditioning. How do the lipids and the omega-3's fit into this whole story?

DR. IAIZZO:

Well, the omega-3's have been implicated for years and there were lot of epidemiologic studies where they looked at different populations throughout the world and showed that individuals that have a high omega-3 diet basically have less incidents of heart disease and using our animal model, we thought well we could also investigate omega-3 fatty acids. One of the unique properties

© 2023 ReachMD

though of the omega-3 is if you start giving them in high concentrations intravenously, they will actually be hemolytic, so that might be a negative thing. So the thought was that we could do this basically in the pericardial space and to do more targeted delivery. So we recently published an article where we were able to deliver omega-3 fatty acids to pericardial space and our ischemia reperfusion model in the swine, we were able to show that during the ischemia, we reduced arrhythmias by 50% and subsequently (12:00) reduced infarct sizes by 50%. So, our lab is continuing on with this line of investigation and trying to look at more long-term followup studies.

DR. MATTHEW SORRENTINO:

I want to thank Dr. Iaizzo for being our guest. We have been discussing the Visible Heart Laboratory at the University of Minnesota, which is a unique laboratory for heart research and heart education.

I am Dr. Matthew Sorrentino and you have been listening to a special segment on medical education on ReachMD XM 157, the channel for medical professionals. To comment or listen to our full library of podcast, visit us at www.reachmd.com register with the promo code radio and receive six months' free streaming for your home or your office and thank you for listening.

© 2023 ReachMD